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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/521,761	01/21/2005	Tomi Jarvinen	HORMOS-019	2621

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EXAMINER	
GOON, SCARLETT Y	
ART UNIT	PAPER NUMBER
1623	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/521,761	JARVINEN ET AL.	
	Examiner	Art Unit	
	SCARLETT GOON	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 June 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 29 June 2009 has been entered.

This Office Action is in response to Applicants' Remarks filed on 29 June 2009.

Claims 13-21 are currently pending and are examined on the merits herein.

Priority

This application is a National Stage entry of PCT/FI03/00511 filed on 24 June 2003 and claims priority to Finland foreign application 20021545 filed on 29 August 2002. A certified copy of the foreign priority document in English has been received.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 14 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation "cyclodextrin is α-cyclodextrin, β-cyclodextrin, γ-cyclodextrin or a derivative therefore" in claim 14 renders the claim herein indefinite. The recitation of a "derivative" is not clearly defined in the specification, and therefore does not set forth the metes and bounds of the terms "derivative" or "analog". The Merriam-Webster's Online Dictionary defines "derivative" as "a chemical substance related structurally to another substance and theoretically derivable from it" (PTO-892, Ref. U). Hence, one of ordinary skill in the art could not ascertain and interpret the metes and bounds of the patent protection desired as to "cyclodextrin is α-cyclodextrin, β-cyclodextrin, γ-cyclodextrin or a derivative therefore" herein. One of ordinary skill in the art would clearly recognize that a derivative of a cyclodextrin would read on those compounds having any widely varying groups that could be used to substitute the compound. Any significant structural variation to a compound would be reasonably expected to alter its properties; e.g. physical, chemical, physiological effects and functions. Thus, it is unclear and indefinite as to how the "derivative" herein is encompassed thereby.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

> invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 13-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent 6,451,849 B1 to Ahotupa *et al.* (herein referred to as the '849 patent, of record), in view of journal publication by Loftsson *et al.* (PTO-892, Ref. V), in view of U.S. Patent No. 5,336,496 to Akimoto *et al.* (herein referred to as the '496 patent; PTO-892, Ref. A).

The Ahotupa '849 patent teaches methods for prevention of cancers and hormone dependent diseases based on administering an effective amount of hydroxymatairesinol or a geometric isomer or a stereoisomer thereof to said person (column 3, line 66 – column 4, line 4; column 1, lines 14-23). Hydroxymatairesinol is the most abundant plant lignan found in the heartwood of spruce (column 1, lines 53-60). The hydroxymatairesinol can be in the form of a pharmaceutical preparation or a food product (column 4, lines 13-30). The food product can be a functional food, a nutritional supplement, a nutrient, a pharmafood, a nutraceutical, a health food, a designer food or any food product (column 5, lines 17-20).

It is noted that the Ahotupa '849 patent does not explicitly indicate that the pharmaceutical preparation comprising hydroxymatairesinol also includes an acceptable carrier. However, as the Ahotupa '849 patent discloses that hydroxymatairesinol is administered at 3.0 mg/kg to animals in a test for antitumor activity, it is inherent that the pharmaceutical preparation includes a carrier.

It is further noted that the Ahotupa '849 patent does not explicitly teach a dietary supplement composition comprising hydroxymatairesinol and a carrier. However, as the Ahotupa '849 patent does teach that hydroxymatairesinol can be used as a nutritional supplement, it is the Office's position that the nutritional supplement can also function as a dietary supplement.

The teachings of the Ahotupa '849 patent differ from that of the instantly claimed invention in that hydroxymatairesinol is not in the formation of an inclusion complex with cyclodextrin.

Loftsson *et al.* teach that cyclodextrins can interact with appropriately sized molecules to result in the formation of inclusion complexes. These noncovalent complexes offer a variety of physiochemical advantages over the unmanipulated drugs including the possibility for increased water solubility and solution stability (p. 1017, abstract). Additionally, the cyclodextrins can be used to increase bioavailability of the drugs, or be used to convert liquid drugs into microcrystalline powders or prevent drug-drug or drug-additive interactions (p. 1017, column 2, first bridging paragraph). The most common cyclodextrins include the natural cyclodextrins, α-, β-, and γ-cyclodextrin (p. 1017, column 2, second paragraph). The natural cyclodextrins can be modified to increase their water solubility, such as by alkylation or hydroxyalkylation of the cyclodextrin hydroxyl groups (p. 1018, column 1). Examples of modified cyclodextrins are shown in Table 2 (p. 1019, column 1). The most common pharmaceutical application of cyclodextrins is to enhance drug solubility in aqueous solutions (p. 1020, column 2, first paragraph). The solubilizing effects of various cyclodextrins on three different drugs are shown in Table 5 (p. 1021). Cyclodextrins are thus useful as tools to generate aqueous drug solutions without the use of organic cosolvents, surfactants, or lipids, as formulation adjuncts which increase dissolution rates and oral bioavailability of solid drug complexes, and as materials used to generate safe iv dosage forms intended to provide important pharmacokinetic information or act as potential drug products per se (p. 1024, column 2).

The Akimoto '496 patent teaches a composition for inhibiting Δ^5-desaturase comprising an effective ingredient selected from the group consisting of lignan

compounds, curcumin and piperonyl butoxide. As the lignan compounds, sesamin, sesaminol, episesamin, episesaminol, sesamolin, 2-(3,4-methylenedioxyphenyl)-6-(3-methoxy-4-hydroxyphenyl)-3,7-dioxabicyclo[2.2.0]octane, 2,6-bis-(3-methoxy-4-hydroxyphenyl)-3,7-dioxabicyclo[3.3.0]octane, and 2-(3,4-methylenedioxyphenyl)-6-(3-methoxy-4-hydroxyphenoxy)-3,7-dioxabicyclo[3.3.0]-octane are used (column 2, lines 14-22). These lignan compounds have also been shown to have possible application for inhibition of lipid peroxidation *in vivo*, which is considered a cause of senility, oncogenesis and the like (column 1, lines 47-50). The compounds may be converted to inclusion bodies with cyclodextrin, which are then formulated to powders, particles, tablets and other conventional formulations (column 4, lines 5-9).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of the Ahotupa '849 patent, concerning a composition comprising hydroxymatairesinol for use in the prevention of cancer and hormone dependent diseases, with the teachings of Loftsson *et al.*, regarding the ability of cyclodextrin to form inclusion complex with various drugs, thereby increasing their water solubility, solution stability, and/or bioavailability, with the teachings of the Akimoto '496 patent, regarding the complexation of lignans into inclusion bodies with cyclodextrin. One would have been motivated to combine the teachings in order to receive the expected benefit, as suggested by Loftsson *et al.*, that cyclodextrins improve the water solubility, solution stability, and/or bioavailability of drugs. With regards to the specific cyclodextrin for forming an inclusion complex, since Loftsson *et al.* teach that cyclodextrins interact with appropriately sized molecules, which is also dependent on

the hydrophobic, hydrophilic, and charge of the cyclodextrin and guest drug, it is considered within the capabilities of one of ordinary skill of the art to select the cyclodextrin which would form the most effective inclusion complex. Furthermore, as the Akimoto '496 patent suggests the formation of inclusion complexes with lignans that bear similar structural motifs to hydroxymatairesinol, one of ordinary skill in the art would reasonably expect success in the formation of an inclusion complex of hydroxymatairesinol with cyclodextrin.

Thus, the claimed invention as a whole is *prima facie* obvious over the combined teachings of the prior art.

Response to Arguments

Applicant's arguments, filed 29 June 2009, with respect to the rejection of claims 13-21 made under 35 USC § 103(a) as being unpatentable over U.S. Patent No. 6,451,849 to Ahotupa *et al.*, in view of U.S. Patent No. 6,559,168 to Marfat *et al.*, have been fully considered but are moot in view of the modified rejection above.

Applicants argue that the Marfat '168 patent is directed to PD4E inhibitors, and only briefly mentions two lignans which act as PD4E inhibitors, both of which are structurally different from hydroxymatairesinol. Additionally, Applicants argue that the Marfat '168 patent does not suggest the combination of hydroxymatairesinol and cyclodextrin. Thus, one of ordinary skill in the art would not have a reasonable expectation of success in complexing hydroxymatairesinol with cyclodextrin based on the teachings of the Marfat '168 patent. These arguments are not persuasive in view of

the modified teachings above. Specifically, as indicated in the rejection above, the Akimoto '496 patent suggest the complexation of lignans, which are structurally similar to hydroxymatairesinol, with cyclodextrins. Therefore, one of ordinary skill in the art would have a reasonable expectation of success in complexing hydroxymatairesinol with cyclodextrin. The teachings of Loftsson *et al.* further provide the motivation for one of ordinary skill in the art to form inclusion complexes of lignans with cyclodextrin, to improve the water solubility, solution stability, and/or bioavailability of the lignans. Thus, as indicated in the rejection above, the claimed invention as a whole is *prima facie* obvious over the combined teachings of the prior art.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SCARLETT GOON whose telephone number is 571-270-5241. The examiner can normally be reached on Mon - Thu 7:00 am - 4 pm and every other Fri 7:00 am - 12 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Shaojia Anna Jiang/
Supervisory Patent Examiner, Art Unit 1623

SCARLETT GOON
Examiner
Art Unit 1623